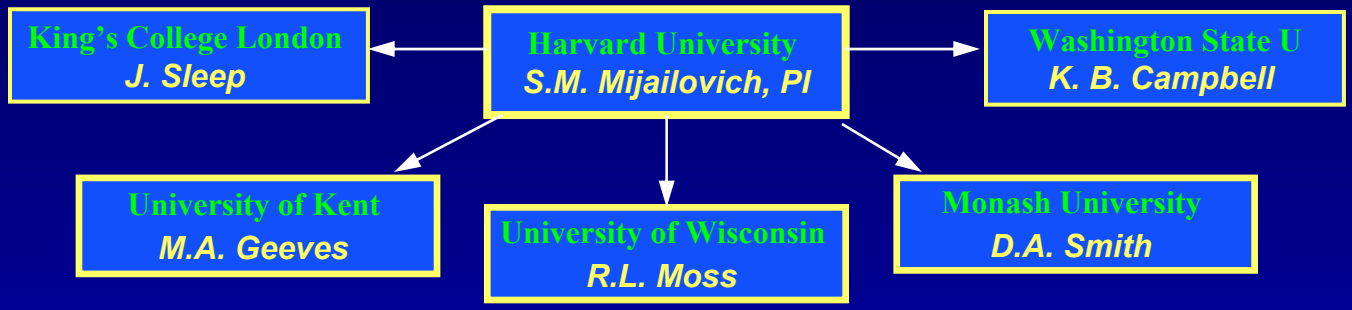
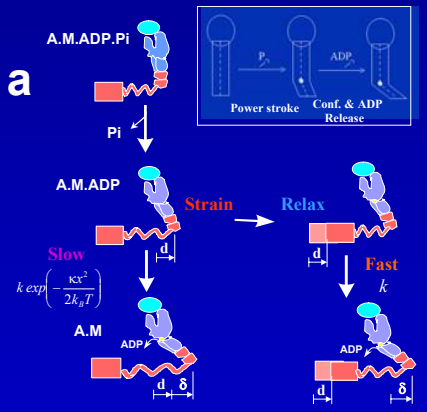
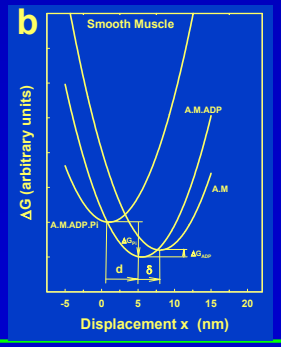
Quantitative Bioengineering Analysis of Muscle Mechanics and Metabolism

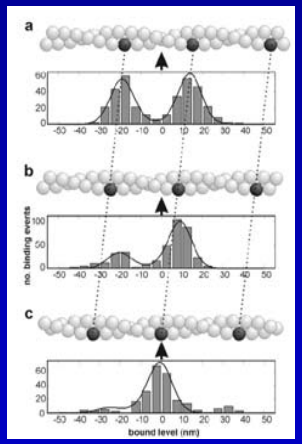
To build a comprehensive computational platform describing muscle contractile function from molecular (protein) interactions to model cells, tissues and organs

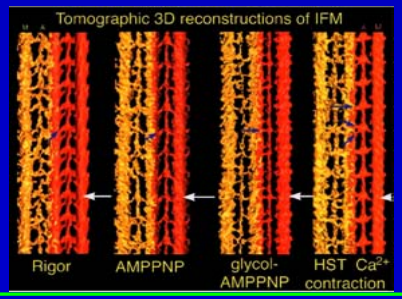
The principal issues: (i) cross-bridge kinetics, (ii) calcium regulation, and (iii) extensible sliding filaments

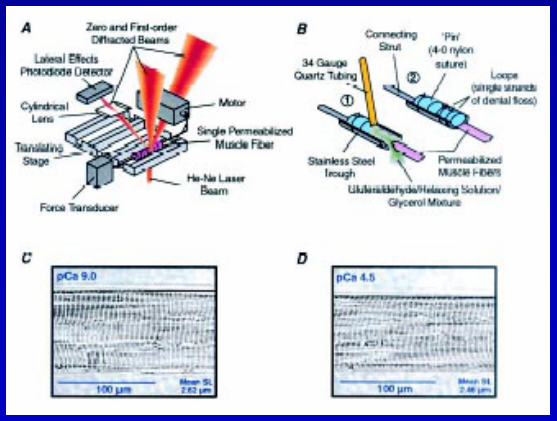


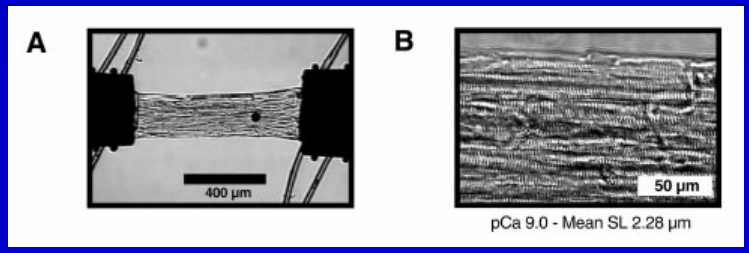












NIAMS: 1 RO1 AR048776-01 A1

Underlying Molecular Processes: Muscle Type Specific

Skeletal Muscle

Cardiac Muscle

Smooth Muscle

Molecular Cell Biology: Membrane Associated Proteins, Signaling Pathways, Genetics

Regulation

Regulatory Proteins
Excitation-Contraction Coupling

Thin Filament Regulation

Phosphorylation of MLC_{20} Thin Filament Proteins

Cross-Bridge Kinetics

Actomyosin Biochemistry
Motility Assays

Cell Architecture

Sarcomere Architecture

Cytoskeleton Remodeling

Sliding Filaments

Filament Extensibility
Sarcomere Geometry

Contraction Stability

Physiological Dynamic Load

Predictions of Physiological Models

Unresolved Problems in Physiology and Medicine

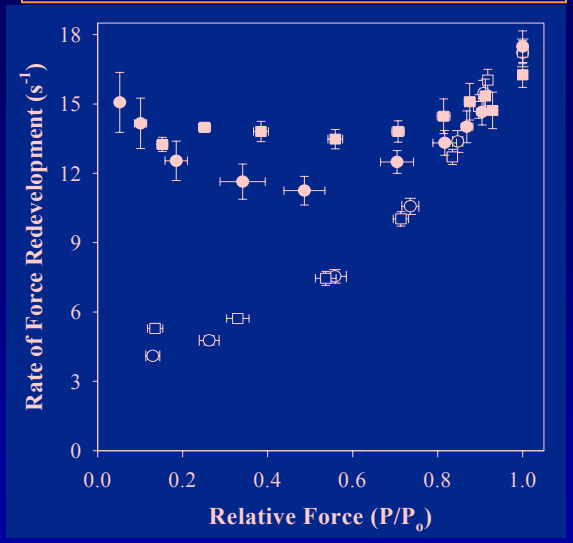
Build Understanding of Diseases in Search for Cure

Critical Testing of our Thinking

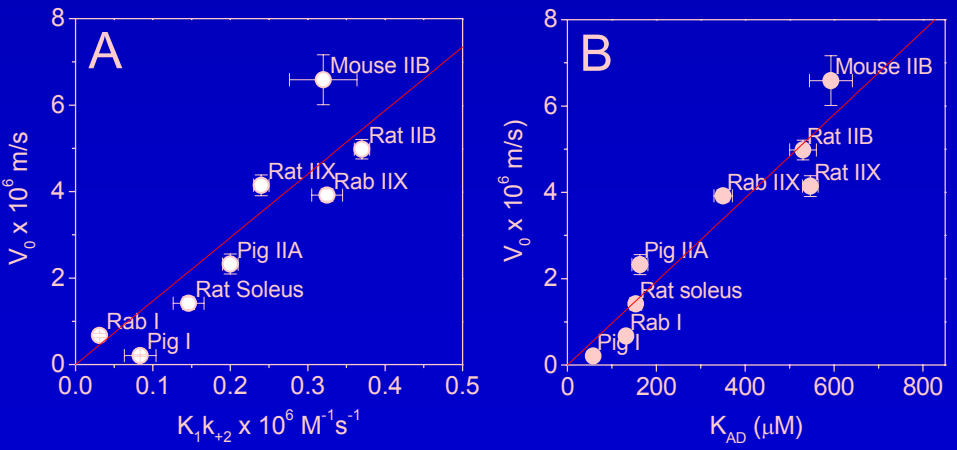
Novel Hypothesis Generation

Design of Critical Experiments

Effects of NEM-S1 on the activation-dependence of k_{tr} in wild-type and transgenic myocardium



Max shortening velocity, V_{max}, vs. the rate constant for ATP dissociation (A); and V_{max} vs. affinity of ADP for S1 (B)



Simulation of T1-T2 transient with extensible actin and myosin filaments